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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/875,520	06/06/2001	Phillip R. Hawkins	PF-0059-5 CON	6922

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	10

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/875,520	HAWKINS ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,24 and 28-44* is/are pending in the application.

4a) Of the above claim(s) *2,24,29,32,34,35,38,43 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,30,31,33,36,37 and 39-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparison A* .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group III, drawn to antibodies which bind to SEQ ID NO: 2 in Paper No. 8, 10/30/2002 is acknowledged. The elected Group reads on claims 28, 30-31, 33, 36-37, 39-42. The methods of claims 35 and 38 drawn to the making of antibodies which bind SEQ ID NO: 2 have been rejoined for examination. The traversal is on the ground(s) that the methods of Groups IV, VII and VIII are drawn to methods of use of the antibody which binds SEQ ID NO: 2, and should be examined together because it would not impose an undue burden on the Examiner. This is not found persuasive for the following reasons.

Applicant's attention is directed to MPEP 808.02 which states that "Where the related inventions as claimed are shown to be distinct under the criteria of MPEP 806.05 (c-i), the examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation one of the following: (A) Separate classification thereof; (B) A separate status in the art when they are classifiable together; (C) A different field of search.". As set forth in the Restriction requirement of Paper No. 7, 10/02/02, Group I is classified in class 930, subclass 10; Group II is classified in class 435 , subclass 7.1, Group IV is classified in class 435, subclass 4; Group VII is classified in class 435, subclass 23.5. The separate classification established for each Group demonstrates that each distinct Group has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. Additionally, elected Group III is related to Group IV as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used

in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody can be used as an inhibitor of GIPL. Thus, the Restriction requirement is proper.

Pursuant to MPEP 821.04, since Applicant has elected claims directed to the product, and in the event the product claims are subsequently found allowable, the withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claims will be rejoined. The requirement is still deemed proper and is therefore made FINAL. Claims 28, 30-31, 33, 35-42 are under consideration. Claims 2, 24, 29, 32, 34-35, 38, 43-44 are withdrawn from consideration pursuant to 37 CFR 1.142(b).

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28, 30-31, 33, 35-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody which binds SEQ ID NO: 2, or comprising an immunogenic fragment of SEQ ID NO: 2, does not reasonably provide enablement for an antibody which binds a naturally-occurring amino acid sequence which is 90% identical to SEQ ID NO: 2, or comprising a biologically active fragment or immunogenic fragment of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 28, 30-31, 33, 35-42 are overly broad since insufficient guidance is provided as to which of the myriad of variant antigenic polypeptides encompassed by the claims which will

retain the characteristics of the GIPL polypeptide. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of GIPL. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

Since the claims encompass antibodies which bind variant polypeptides and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The claims as written do not set forth a functional limitation for the polypeptides encompassed by the claims to which the antibodies are directed. Since the amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the

structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims.

Claims 28, 30-31, 33, 35-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The claims are drawn to antibodies that bind variant polypeptides. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the encoded SEQ ID NO: 2. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify

members of the genus, and because the genus is highly variant, the polypeptide of SEQ ID NO: 2 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 28, 31, 33, 35-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Baylink et al (WO 93/15107).

Balink et al. teaches antibodies which bind to peptides derived from the amino terminal of human type I collagen (page 4, lines 1-10). These peptides have six amino acids in common with the polypeptide of SEQ ID NO: 2 disclosed in the instant application (see Sequence Comparison A, attached). Since antibodies only need six amino acids in common to recognize an epitope, the antibodies taught in Baylink et al. will specifically bind to the polypeptide of SEQ ID NO: 2, thus claims 28 is anticipated. Baylink et al. further teaches compositions of the antibody in buffers, and antibodies that are labeled (page 17, lines 20-30), thus claims 31, 33 are anticipated.

Claims 36-37, 39-42 are product by process claims. Patentability of a product-by-process claim is determined by the novelty and nonobviousness of the claimed product itself without consideration of the process for making it which is recited in the claims. *In re Thorpe*, 227

USPQ 964 (Fed. Cir. 1985). In the instant case, the antibodies taught by Baylink et al. meet the limitations for specificity as set forth in the claims, thus claims 36-37 are anticipated. Claims 39-42 are anticipated because Baylink et al. teaches monoclonal antibodies which bind the amino terminal of human type I collagen (page 4, lines 1-10).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28, 30-31, 33, 35-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baylink et al. (WO 93/15107) in view of U.S. Patent No. 5,530,101 (Queen et al.).

The disclosure of Baylink et al. has been set forth above. Baylink et al. differs from the instant invention by not disclosing human, humanized or single-chain antibodies to GIPL. U.S. Patent No. 5,530,101 discloses that non-human antibodies do not fix complement as well as human antibodies, thus necessitating the humanization of antibodies produced in other species (column 1, line 38), this also indicates the superiority of human antibodies. U.S. Patent No. 5,530,101 discloses the humanization of antibodies (column 2, lines 1-8). Humanized antibodies are disclosed as being important because they bind to the same antigen as the original antibodies, but are less immunogenic when injected into humans. U.S. Patent No. 5,530,101 discloses that immunoglobulins may exist in a variety of other forms, including, *inter alia*, single chains. Therefore, it would have been obvious to one of skill in the art at the time the invention was

made to produce either anti-GIPL antibodies, to humanize anti-GIPL antibodies, or to produce single chain anti-GIPL antibodies.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
September 30, 2003

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